POSTER SESSION

DRUG ABUSE II

TUESDAY, AUGUST 20 - 12:45 PM

GRAND BALLROOM

70 605

INTERRELATIONS AMONG PSYCHOPHARMACOLOGIC DRUGS: CLUSTER ANALYSIS OF OPIATE DRUGS IN A SYMPTOM SPACE.

Charles Haertzen and Karen Kumor (SPON: Donald Jasinski), NIDA Addiction Research Center, Baltimore, MD 21224.

Two models of the relative psychopharmacologic differences among four opiate drugs and placebo were developed in order to help conceptualize the relationship of opiate drugs to each other in man. Subjects received a series of opiate drugs, ketocyclazocine 1.2 mg, morphine 30 mg, cyclazocine 1.0 mg, naloxone 300 mg, and placebo. Two independent sets of data were gathered from each subject; one data set was the Addiction Research Center Inventory, the other a new digital scale on which the subject rated an unknown drug's similarity to each drug in an unidentified series given previously. Each data set was analyzed separately using a discriminative analysis procedure which calculates a sum of t-squares between drug conditions to obtain quantities which are representative of distances between drug pairs. The resultant figures from the two methods are similar to each other (r = .66), and show that morphine and ketocyclazocine are distant from each other, cyclazocine and ketocyclazocine are close to each other, and large doses of naloxone while closest to placebo are displaced from placebo toward morphine.

71 606

KETANSERIN AND PIRENPERONE ATTENUATE ACUTE MORPHINE WITHDRAWAL-INDUCED SUPPRESSION OF FOOD-REINFORCED AUTOSHAPED BEHAVIOR.

B.S. Neal* and S.B. Sparber, Dept. of Pharmacology, University of Minnesota, Minneapolis, MN 55455.

We have reported that the antidepressant agent mianserin (MIA) is effective in attenuating many signs of morphine withdrawal. To strengthen the argument that MIA is influencing serotonergic mechanisms to exert its anti-withdrawal effects, we looked at the ability of other structurally dissimilar 5-HT antagonists, ketanserin (KET) and pirenperone (PIR), to attenuate the acute morphine withdrawal syndrome. Rats, autoshaped and making 35 or 36 lever-touch responses (36 trials), were injected with naloxone (5 mg/kg) 4 hr after a single dose of morphine sulfate (20 mg/kg), when conditioned behavior had returned to control rates (EJP, 90, 269, 1983). KET (0.125-1.25 mg/kg) was able to attenuate the Nx-induced behavioral suppression. Only the lowest dose of PIR tested (0.01 mg/kg) was able to block the behavioral suppression and also block Nx-induced hypothermia. Higher doses (0.025-0.25 mg/kg) tended to bring responding back down and may be acting through other receptor populations (EJP, 103, 169, 1984). These data support the hypothesis that MIA is exerting its anti-withdrawal effect through serotonergic mechanisms as KET and PIR are also effective in attenuating morphine withdrawal. (Supported by USPHS grant DA01880.)

72 607

The Effects of Atropine and Scopolamine on Rewarding Brain Stimulation.

J.W. Kemp, Jr.,* G.T. Bain* and C. Kornetsky. Laboratory of Behavioral Pharmacology, Boston University School of Medicine, Boston, MA 02118

Many drugs of abuse lower the threshold for rewarding brain stimulation in the rat. This threshold lowering effect has been proposed as a model of drug-induced euphoria. Since it has been reported that atropine and scopolamine are abused (e.g., O'Grady, et al., Milit. Med., 148, 1983), the present study was undertaken to assess the effects of these two anticholinergic agents. Thresholds for reinforcing electrical stimulation to the medial forebrain bundle-lateral hypothalamus were determined by means of a rate-free psychophysical method. Low to moderate doses of atropine (2.0-32 mg/kg, i.p.) and scopolamine (0.125-0.25 mg/kg, i.p.) were found to have no significant effect on reward thresholds, whereas the higher doses examined (atropine, 64 mg/kg; scopolamine, 0.50 mg/kg and 1.0 mg/kg) were found to raise reward thresholds without affecting the animals ability to perform the task. These results suggest that unlike the opioids and psychomotor stimulants the abuse of anticholinergics is not related to a primary effect on the brain reward system.

(Supported in part by NIDA grant DA 02326 and NIDA Research Scientist Award (CK) K05 DA 00090).

73 608

The Effects of Ethanol and Δ9-THC on Rewarding Brain Stimulation.

E.M. Unterwald* and C. Kornetsky. Lab. Behav. Pharmacol., Boston Univ. Sch. Med., Boston, MA 02118.

Increased sensitivity to rewarding brain stimulation has been used as an animal model of drug-induced euphoria. Many abused substances lower the threshold for brain-stimulation reward. The widespread abuse of marijuana along with alcoholic beverages prompted us to study the effects of co-administration of Δ9-THC and ethanol. Ethanol (.025-1.6 g/kg) caused no significant changes in the threshold for rewarding stimulation to the medial forebrain bundle-lateral hypothalamus in the rat. Likewise, Δ9-THC (.08-1.25 mg/kg) also had no effect. Higher doses of either agent completely abolished performance. Concomitant administration of 0.4 g/kg of ethanol with various doses of Δ9-THC potentiated this performance deficit, shifting the dose response curve to the left. This suggests that small amounts of ethanol may increase the behavioral toxicity of Δ9-THC. Further, the results from this experiment indicate that, unlike opiates and CNS stimulants, the reinforcing effects of ethanol and Δ9-THC are not mediated through activation of the pathways involved in brain stimulation reward.

(Supported in part by NIAA grant AA05950, AA05221 (EMU) and NIDA Research Scientist Award (CK) K05 DA 00099).

74 609

EFFECTS OF NEONATAL delta-9-TETRAHYDROCANNABINOL (THC) ON ADULT BRAIN BIOGENIC AMINE TURNOVER FOLLOWING STRESS IN MALE FISCHER-344(CDF) RATS.

D.J. Mokler, S.E. Robinson, J.H. Johnson and J.A. Rosecrans, Depts. Pharmacol. and Anat., Va. Commonwealth Univ., Richmond, VA 23298

Male CDF rats (litter-mates) were administered 10 mg/kg of THC (s.c.) or vehicle on 4,6 and 8 days of age. At day 130 rats were conditioned to an 8-day foot-shock-induced analgesia (FSIA) paradigm. All rats were sacrificed on day 8, 15 min. after exposure to the shock environment only. The results of these studies indicated that rats can be conditioned behaviorally to FSIA which can also be observed by an activation of the pituitary-adrenal axis and alterations of both brain area 5-HT (5HIAA/5HT) and DA (DOPAC/DA) turnover. THC had no effect on either neuroendocrine or 5-HT turnover. THC, however, did significantly alter frontal cortex DA turnover. The effect was not seen as a reduction of the overall stressed-induced increase in DOPAC, but a reduction of both DA and DOPAC suggesting that neuronal flow to the FC was slowed down in adults rats given THC during postnatal development. (Supported by NIDA grant DA-07027.)